

**REMARKS**

This is in response to the Office Action that was mailed on August 7, 2002. Applicants gratefully acknowledge the Examiner's indication that this application contains allowable subject matter. Claims 1 and 2 are amended to disclaim compounds taught by the prior art, and to exclude embodiments of the present invention now claimed in new claim 17. Claim 4 is corrected as suggested by the Examiner. New claims 13-16 recite preferred embodiments of claim 4. No additional new subject matter is introduced by this Amendment. Claims 1, 2, 4, and 6-17 are in the case.

**Rejection Under 35 U.S.C. §112**

Claims 1, 4, 6, and 12 were rejected under the second paragraph of 35 U.S.C. §112 as allegedly failing to define the invention properly. The Examiner raised impliedly suggested that the adjective "pharmacologically" in claim 4 be replaced by the adjective "pharmaceutically". Applicants have made the suggested substitution. The Examiner referred to an allegedly "duplicated citation in the claim 1". Applicants have amended generic claim 1 and subgeneric claim 2 to make them easier to construe. It is respectfully submitted that the claims as amended fully satisfy the requirements of the statute.

**Rejections Under 35 U.S.C. §102**

Claims 1, 2, 4, and 7 were rejected under 35 U.S.C. §102 as allegedly being anticipated by Cho et al, Behrens, and Lerch. These rejections are obviated by the disclaimers recited in claims 1 and 2 as amended.

**Rejection Under 35 U.S.C. §103**

Claims 1, 2, 4, 7, and 10 were rejected under 35 U.S.C. §103 as allegedly being obvious from Simmonds. This ground of rejection is respectfully traversed. The presently claimed compounds are admittedly different in structure from the compounds of the reference. The reference teaches that its compounds have CNS activity. Nothing in the Simmonds reference or in the knowledge base of those having ordinary skill in the art suggests that Applicants' "variants" of the Simmonds compounds would have serotonin receptor and muscle relaxant activity. It is by now axiomatic in U.S. patent law that a compound and its properties are inseparable. Accordingly, the record fails to establish a *prima facie* case of obviousness against the novel serotonin receptor/muscle relaxant compounds presently claimed.

**Conclusion**

Should there be any issues remaining in this application that require discussion, the Examiner is invited to contact Mr. Richard Gallagher, Registration No. 28,781, at (703) 205-8008.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit

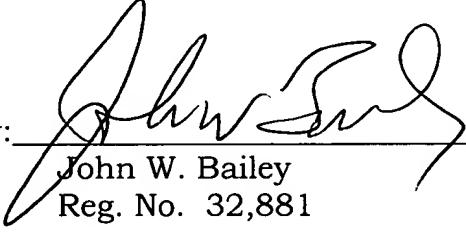
Appl. No.: 09/852,850


Account No. 02-2448 for any additional fees required under 37 C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By: \_\_\_\_\_

  
John W. Bailey  
Reg. No. 32,881

JWB/RG 

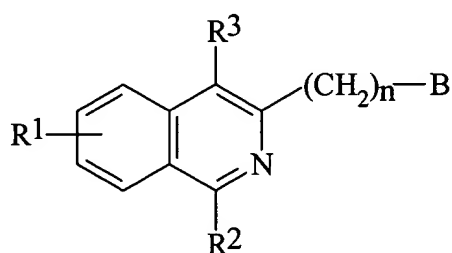
P. O. Box 747  
Falls Church, VA 22040-0747  
(703) 205-8000

Enclosure:

Marked Up Version of Claims Showing Amendments.

**Marked Up Version of Claims Showing Amendments:**

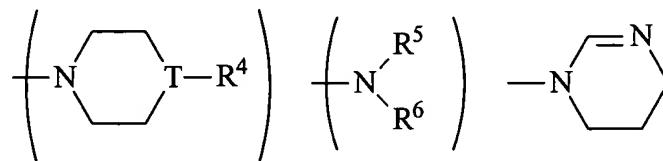
1. (twice amended) A condensed pyridine compound represented by the following formula, its pharmaceutically acceptable salt or hydrates thereof



wherein,

R<sup>1</sup> represents a hydrogen atom, a halogen atom, a lower alkyl group or a lower alkoxy group;

R<sup>2</sup> represents a 4-morpholinyl group, a 1-imidazolyl group, a 1-lower alkyl homopiperazin-4-yl group or a group selected from the groups represented by the following formulae:



(wherein, T represents a nitrogen atom or a methine group;

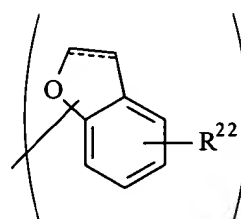
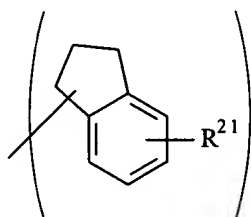
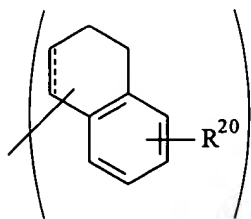
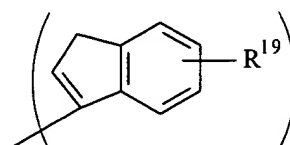
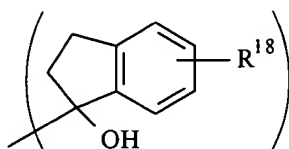
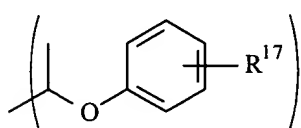
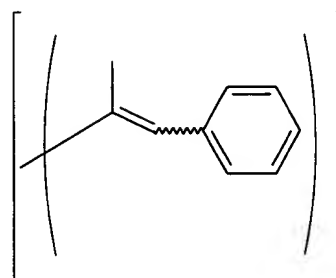
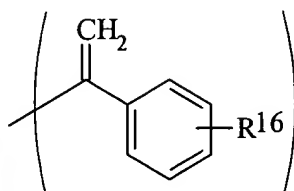
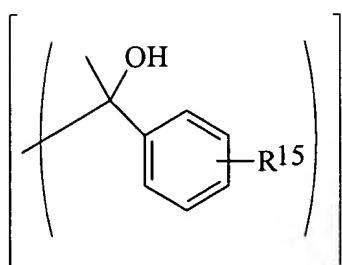
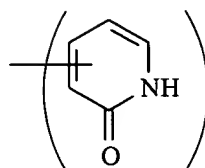
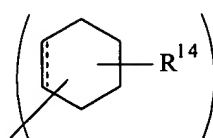
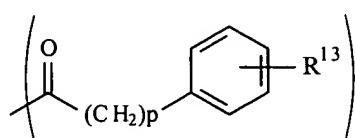
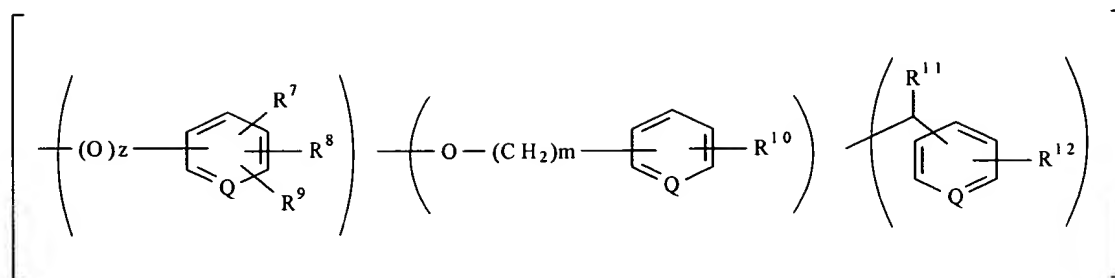
R<sup>3</sup> represents a hydrogen atom, a halogen atom, a lower alkyl group or a lower alkoxy group;

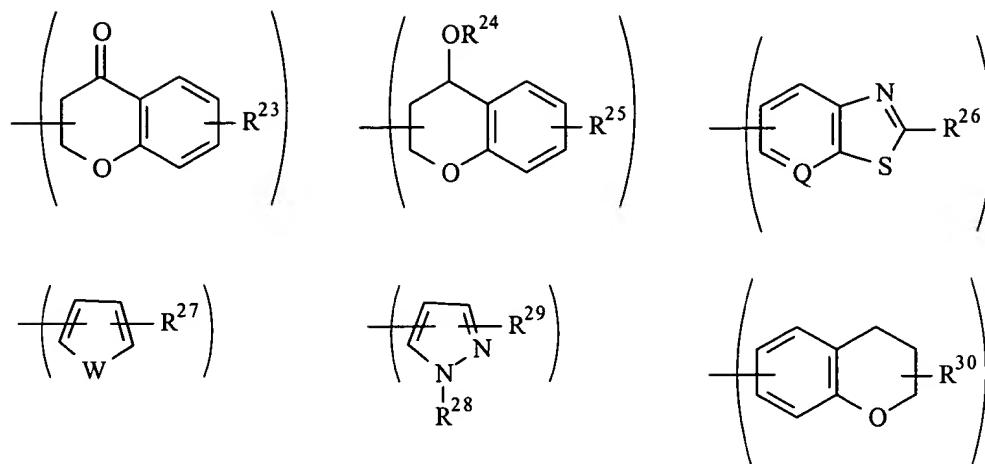
R<sup>4</sup> represents a hydrogen atom, a lower alkyl group, a hydroxy lower alkyl group, a halogenated lower alkyl group, a lower cycloalkyl group, an aryl group, an aralkyl group, 1-piperidyl group, an alkenyl group, a cyano lower alkyl group, a carbamoyl lower alkyl group, a lower acyl group, an aromatic acyl group, a lower alkoxyl carbonyl group, an aryloxycarbonyl group or an aralkyloxycarbonyl group;

R<sup>5</sup> and R<sup>6</sup> are the same as or different from each other and each represents a hydrogen atom, a lower alkyl group, a di lower alkyl aminoalkyl group, an optionally substituted heteroaryl lower alkyl group);

n represents 0 or an integer of 1 to 6; and

B represents an optionally substituted aryl group, an optionally substituted heteroaryl group, an optionally substituted aralkyloxy group, an aryl(hydroxy)alkyl group, an aromatic acyl amino group, an arylsulfonylamino group, a lower alkoxyl arylsulfonylamino group, a hydroxy lower alkoxyl styryl group, a lower alkoxyl aryloxy group, 4-phenylpiperidin-1-yl group, 4-pyridylpiperidin-1-yl group, an optionally substituted arylalkenyl group, an optionally substituted arylalkynyl group, an optionally substituted heteroarylalkenyl group, an optionally substituted heteroarylalkynyl group, an aromatic acyl alkynyl group, an optionally N-substituted amino lower alkyl group, an optionally substituted arylamino group, an optionally substituted aralkylamino group or a group selected from the groups represented by the following formulae:





(wherein  $[z]$  represents 0 or 1;

$Q$  represents a nitrogen atom or a methine group;

$R^7$ ,  $R^8$  and  $R^9$  are the same as or different from each other and each represents a hydrogen atom, a halogen atom, hydroxyl group, a lower alkyl group, a lower alkenyl group, a lower alkynyl group, a lower alkoxy group, a lower thioalkoxy group, a hydroxy lower thioalkoxy group, an arylthio group, a heteroarylthio group, a heteroaryl(hydroxy)alkyl group, a halogenated lower alkyl group, a hydroxy lower alkyl group, a dihydroxy lower alkyl group, a halogenated (hydroxy) lower alkyl group, a hydroxyalkenyl group, a hydroxyalkynyl group, a hydroxy lower cycloalkenyl group, a lower alkoxy(hydroxy)alkyl group, a lower alkoxy(hydroxy)alkoxy group, a lower alkoxyalkyl group, a lower alkoxyalkoxy group, a lower thioalkoxyalkoxy group, a lower alkylsulfonylalkoxy group, a hydroxy lower alkoxy group, a dihydroxy lower alkoxy group, a hydroxy lower alkylalkoxy group, a hydroxyimino lower alkyl group, a lower cycloalkyl (hydroxy) alkyl group, an aralkyl group, a hydroxyaralkyl group, cyano group, a cyano lower alkyl group, amide group, an N-lower alkylamide group, an N-lower cycloalkylamide group, an N,N-di lower alkylamide group, an N-hydroxy

lower alkylamide group, an N-hydroxy lower alkyl-N-lower alkylamide group, an N-arylamide group, cyclic aminocarbonyl group, carbamoyl group, an N-lower alkyl carbamoyl group, an N,N-di lower alkyl carbamoyl group, aminosulfonyl group, cyclic aminosulfonyl group, an N-lower alkylaminosulfonyl group, an N-lower cycloalkylaminosulfonyl group, an N,N-di lower alkylaminosulfonyl group, an N-hydroxy lower alkylaminosulfonyl group, an N-lower alkoxyalkylaminosulfonyl group, an N-halogenated lower alkylsulfonyl group, pyrrolidinylsulfonyl group, a lower alkylsulfonylaminoalkyl group, an N-lower alkylaminosulfonylalkyl group, an N,N-di lower alkylaminosulfonylalkyl group, a lower acyl group, a lower acylalkyl group, a lower cycloalkyl(hydroxy)methyl group, tetrahydropyranyl group, hydroxytetrahydropyranyl group, a hydroxy lower alkyltetrahydropyranyl group, a lower acylaminoalkyl group, (thiazol-2-yl)hydroxymethyl group, di(thiazol-2-yl)hydroxymethyl group, a lower alkylsulfonyl group, a lower alkoxyalkylsulfonyl group, a hydroxy lower alkylsulfonyl group, a lower alkylsulfonylalkyl group, an N-lower alkylamidealkyl group, an aryl group, an aralkyl group, a heteroaryl group, a heteroaryl lower alkyl group, a heteroaryl lower alkoxy group, a heteroarylsulfonyl group, 4-morpholinylsulfonyl group, 4-oxythiomorpholinylsulfonyl group, 4-dioxythiomorpholinylsulfonyl group, 4-morpholinylsulfonyl group, a hydroxy lower cycloalkyl group, a hydroxy lower cycloalkyloxy group, a hydroxycycloalkenyl group, a halogenated hydroxy lower alkyl group, 4-hydroxypiperidyl group, a 4-lower alkoxypiperidyl group, an  $\omega,\omega$ -lower alkylenedioxyalkyl group, an  $\omega,\omega$ -lower alkylenedioxyalkoxy group, a lower cycloalkylhydroxymethyl group, an aryloxy group, an arylaminosulfonyl group, amino group, a lower alkylamino group, a di lower alkylamino group, a hydroxy lower alkylamino group, a lower acylamino group, a hydroxy lower acylamino group, a lower alkylsulfonylamino group, a pyridyl lower alkoxy



group, a lower alkylpyridylalkoxy group, a lower alkoxyhydroxyalkoxy group, a lower thioalkoxyalkoxy group, a lower alkylsulfonylalkoxy group, an N-lower alkylcarbamoyl group, an N,N-di lower alkylcarbamoyl group, an N-hydroxy lower alkylcarbamoyl group, an N-hydroxy lower alkyl-N-lower alkylcarbamoyl group, a halogenated lower alkoxy group, a cyano lower alkoxy group, a hydroxy lower cycloalkoxy group, trifluoromethyl group, trifluoromethoxy group, an amino lower alkoxy group, an N-lower alkyl aminoalkoxy group, an N,N-di lower alkylaminoalkoxy group, a lower acylalkoxy group, a lower acylaminoalkoxy group, a (1,3-dioxolanyl) lower alkyl group, a (1,3-dioxolanyl) lower alkoxyl group, an amide lower alkoxyl group, a 4-(hydroxyalkyl)tetrahydropyran-4-yl group, 2,3-dihydrobenzofuranyl group, a 2-hydroxy-2-alkyl-2,3-dihydrobenzofuranyl group, indanonyl group, hydroxyindanyl group, an imidazolyl lower alkoxyl group, succinimide group or 2-oxazolidon-3-yl group;

furthermore, R<sup>7</sup> represents a hydrogen atom, while R<sup>8</sup> and R<sup>9</sup> form cyclopentanone ring, hydroxycyclopentane ring, a hydroxyalkylcyclopentane ring, cyclohexanone ring, hydroxycyclohexane ring, a hydroxyalkylcyclohexane ring, 2-hydroxymethyl-2-methylcyclopentanone ring, 1,2-ethylenedioxy ring or methylenedioxy ring;

m or] p represents 0 or an integer of 1 to 6;

[R<sup>10</sup>, R<sup>12</sup>,] R<sup>13</sup>, R<sup>14</sup>, [R<sup>15</sup>,] R<sup>16</sup>, R<sup>17</sup>, R<sup>18</sup>, R<sup>19</sup>, R<sup>20</sup>, R<sup>21</sup>, R<sup>22</sup>, R<sup>23</sup>, R<sup>25</sup>, R<sup>27</sup> and R<sup>29</sup> independently represent a hydrogen atom, a halogen atom, hydroxyl group, a lower alkyl group, a lower alkoxy group, a hydroxy lower alkyl group, a hydroxy lower alkoxy group or tetrahydropyranyl group;

[R<sup>11</sup> represents a hydrogen atom, a halogen atom, hydroxy group, a lower alkyl

group or a lower alkoxy group;]

R<sup>24</sup> represents a hydrogen atom or a lower alkyl group;

R<sup>26</sup> represents a hydrogen atom or a hydroxy lower alkyl group;

R<sup>28</sup> represents a hydrogen atom or a lower alkyl group;

R<sup>30</sup> represents a hydrogen atom, a lower alkyl group, a lower alkoxy group, a hydroxy lower alkyl group or a hydroxy lower alkoxy group;

W represents sulfur atom or oxygen atom; and

the bond represented by the following formula:



represents a single or double bond; [and

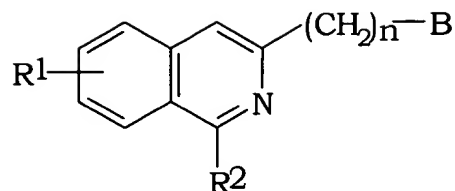
the bond represented by the following formula:



represents trans or cis bond)]

provided that: when n represents 0, B is not 1-naphthyl; when n represents 0 and R<sup>2</sup> is 1-imidazole, B is not phenyl; and when n represents 0 and B is 4-methylpiperidin-1-yl, B is not bromophenyl, chlorophenyl, methoxyphenyl, or tolyl.

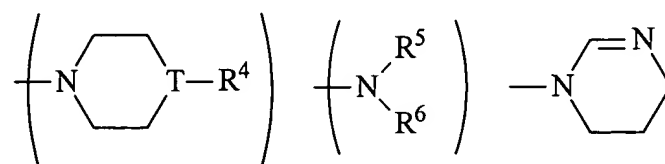
2. (twice amended) A condensed pyridine compound represented by the following formula, its pharmaceutically acceptable salt or hydrates thereof



wherein,

R<sup>1</sup> represents a hydrogen atom, a halogen atom, a lower alkyl group or a lower alkoxy group;

R<sup>2</sup> represents 4-morpholinyl group, 1-imidazolyl group, a 1-lower alkylhomopiperazin-4-yl group or a group selected from the groups represented by the following formulae:



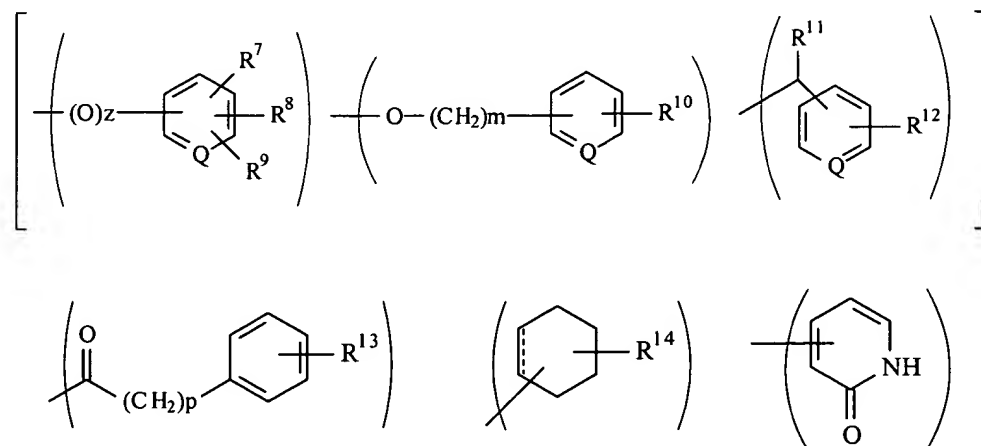
(wherein, T represents a nitrogen atom or a methine group;

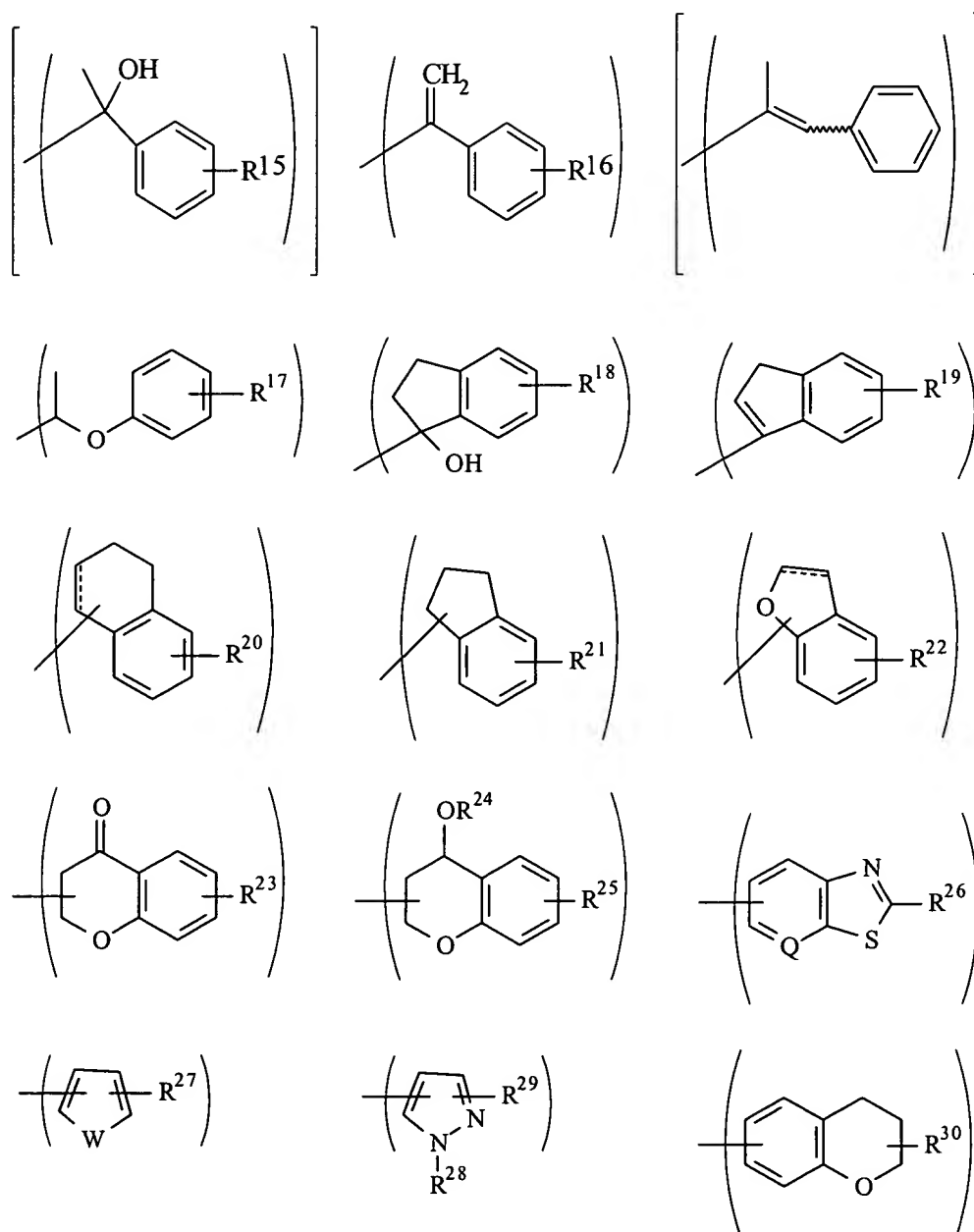
R<sup>4</sup> represents a hydrogen atom, a lower alkyl group, a hydroxy lower alkyl group, a halogenated lower alkyl group, a lower cycloalkyl group, an aryl group, an aralkyl group, 1-piperidyl group, an alkenyl group, a cyano lower alkyl group, a carbamoyl lower alkyl group, a lower acyl group, an aromatic acyl group, a lower alkoxy carbonyl group, an aryloxycarbonyl group or an aralkyloxycarbonyl group; and

R<sup>5</sup> and R<sup>6</sup> are the same as or different from each other and each represents a hydrogen atom, a lower alkyl group, a di lower alkylaminoalkyl group, an optionally substituted heteroaryl lower alkyl group);

n represents 0 or an integer of 1 to 6; and

B represents an optionally substituted aryl group, an optionally substituted heteroaryl group, an optionally substituted aralkyloxy group, an aryl(hydroxy)alkyl group, an aromatic acyl amino group, an arylsulfonylamino group, a lower alkoxy arylsulfonylamino group, a hydroxy lower alkoxy styryl group, a lower alkoxy aryloxy group, 4-phenylpiperidin-1-yl group, 4-pyridylpiperidin-1-yl group, an optionally substituted arylalkenyl group, an optionally substituted arylalkynyl group, an optionally substituted heteroarylalkenyl group, an optionally substituted heteroarylalkynyl group, an aromatic acyl alkynyl group, an optionally N-substituted amino lower alkyl group, an optionally substituted arylamino group, an optionally substituted aralkylamino group or a group selected from the groups represented by the following formulae:





(wherein [z represents 0 or 1;

Q represents a nitrogen atom or a methine group;

R<sup>7</sup>, R<sup>8</sup> and R<sup>9</sup> are the same as or different from each other and each represents a hydrogen atom, a halogen atom, hydroxyl group, a lower alkyl group, a lower alkenyl group, a lower alkynyl group, a lower alkoxy group, a lower thioalkoxy group, a hydroxy lower thioalkoxy group, an arylthio group, a heteroarylthio group, a heteroaryl(hydroxy)alkyl group, a halogenated lower alkyl group, a hydroxy lower alkyl group, a dihydroxy lower alkyl group, a halogenated (hydroxy) lower alkyl group, a hydroxyalkenyl group, a hydroxyalkynyl group, a hydroxy lower cycloalkenyl group, a lower alkoxy(hydroxy)alkyl group, a lower alkoxy(hydroxy)alkoxy group, a lower alkoxyalkyl group, a lower alkoxyalkoxy group, a lower thioalkoxyalkoxy group, a lower alkylsulfonylalkoxy group, a hydroxy lower alkoxy group, a dihydroxy lower alkoxy group, a hydroxy lower alkylalkoxy group, a hydroxyimino lower alkyl group, a lower cycloalkyl (hydroxy) alkyl group, an aralkyl group, a hydroxyaralkyl group, cyano group, a cyano lower alkyl group, amide group, an N-lower alkylamide group, an N-lower cycloalkylamide group, an N,N-di lower alkylamide group, an N-hydroxy lower alkylamide group, an N-hydroxy lower alkyl-N-lower alkylamide group, an N-arylamine group, cyclic aminocarbonyl group, carbamoyl group, an N-lower alkyl carbamoyl group, an N,N-di lower alkyl carbamoyl group, aminosulfonyl group, cyclic aminosulfonyl group, an N-lower alkylaminosulfonyl group, an N-lower cycloalkylaminosulfonyl group, an N,N-di lower alkylaminosulfonyl group, an N-hydroxy lower alkylaminosulfonyl group, an N-lower alkoxyalkylaminosulfonyl group, an N-halogenated lower alkylsulfonyl group, pyrrolidinylsulfonyl group, a lower alkylsulfonylaminoalkyl group, an N-lower alkylaminosulfonylalkyl group, an N,N-di lower alkylaminosulfonylalkyl group, a lower acyl group, a lower acylalkyl group, a lower cycloalkyl(hydroxy)methyl group, tetrahydropyranyl group, hydroxytetrahydropyranyl group, a hydroxy lower alkyltetrahydropyranyl

group, a lower acylaminoalkyl group, (thiazol-2-yl)hydroxymethyl group, di(thiazol-2-yl)hydroxymethyl group, a lower alkylsulfonyl group, a lower alkoxyalkylsulfonyl group, a hydroxy lower alkylsulfonyl group, a lower alkylsulfonylalkyl group, an N-lower alkylamidealkyl group, an aryl group, an aralkyl group, a heteroaryl group, a heteroaryl lower alkyl group, a heteroaryl lower alkoxy group, a heteroarylsulfonyl group, 4-morpholinylsulfonyl group, 4-oxythiomorpholinylsulfonyl group, 4-dioxythiomorpholinylsulfonyl group, 4-morpholinylsulfonyl group, a hydroxy lower cycloalkyl group, a hydroxy lower cycloalkyloxy group, a hydroxycycloalkenyl group, a halogenated hydroxy lower alkyl group, 4-hydroxypiperidyl group, a 4-lower alkoxypiperidyl group, an  $\omega,\omega$ -lower alkylenedioxyalkyl group, an  $\omega,\omega$ -lower alkylenedioxyalkoxy group, a lower cycloalkylhydroxymethyl group, an aryloxy group, an arylaminosulfonyl group, amino group, a lower alkylamino group, a di lower alkylamino group, a hydroxy lower alkylamino group, a lower acylamino group, a hydroxy lower acylamino group, a lower alkylsulfonylamino group, a pyridyl lower alkoxy group, a lower alkylpyridylalkoxy group, a lower alkoxyhydroxyalkoxy group, a lower thioalkoxyalkoxy group, a lower alkylsulfonylalkoxy group, an N-lower alkylcarbamoyl group, an N,N-di lower alkylcarbamoyl group, an N-hydroxy lower alkylcarbamoyl group, an N-hydroxy lower alkyl-N-lower alkylcarbamoyl group, a halogenated lower alkoxy group, a cyano lower alkoxy group, a hydroxy lower cycloalkoxy group, trifluoromethyl group, trifluoromethoxy group, an amino lower alkoxy group, an N-lower alkyl aminoalkoxy group, an N,N-di lower alkylaminoalkoxy group, a lower acylalkoxy group, a lower acylaminoalkoxy group, a (1,3-dioxolanyl) lower alkyl group, a (1,3-dioxolanyl) lower alkoxyl group, an amide lower alkoxyl group, a 4-(hydroxyalkyl)tetrahydropyran-4-yl group, 2,3-dihydrobenzofuranyl group, a 2-hydroxy-2-alkyl-2,3-dihydrobenzofuranyl group, indanonyl group,

hydroxyindanyl group, an imidazolyl lower alkoxyl group, succinimide group or 2-oxazolidon-3-yl group;

furthermore, R<sup>7</sup> represents a hydrogen atom, while R<sup>8</sup> and R<sup>9</sup> form cyclopentanone ring, hydroxycyclopentane ring, a hydroxyalkylcyclopentane ring, cyclohexanone ring, hydroxycyclohexane ring, a hydroxyalkylcyclohexane ring, 2-hydroxymethyl-2-methylcyclopentanone ring, 1,2-ethylenedioxy ring or methylenedioxy ring;

m or] p represents 0 or an integer of 1 to 6;

[R<sup>10</sup>, R<sup>12</sup>,] R<sup>13</sup>, R<sup>14</sup>, [R<sup>15</sup>,] R<sup>16</sup>, R<sup>17</sup>, R<sup>18</sup>, R<sup>19</sup>, R<sup>20</sup>, R<sup>21</sup>, R<sup>22</sup>, R<sup>23</sup>, R<sup>25</sup>, R<sup>27</sup> and R<sup>29</sup> independently represent a hydrogen atom, a halogen atom, hydroxyl group, a lower alkyl group, a lower alkoxy group, a hydroxy lower alkyl group, a hydroxy lower alkoxy group or tetrahydropyranyl group;

[R<sup>11</sup> represents a hydrogen atom, a halogen atom, hydroxy group, a lower alkyl group or a lower alkoxy group;]

R<sup>24</sup> represents a hydrogen atom or a lower alkyl group;

R<sup>26</sup> represents a hydrogen atom or a hydroxy lower alkyl group;

R<sup>28</sup> represents a hydrogen atom or a lower alkyl group;

R<sup>30</sup> represents a hydrogen atom, a lower alkyl group, a lower alkoxy group, a hydroxy lower alkyl group or a hydroxy lower alkoxy group;

W represents sulfur atom or oxygen atom; and

the bond represented by the following formula:

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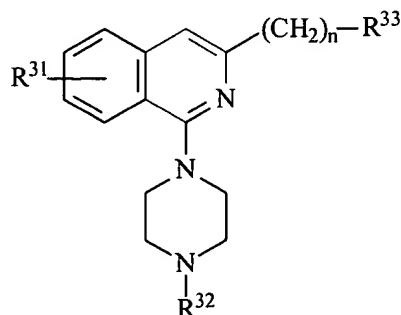
represents a single or double bond; [and  
the bond represented by the following formula:



represents trans or cis bond)]

provided that: when n represents 0, B is not 1-naphthyl; when n represents 0 and R<sup>2</sup> is 1-imidazole, B is not phenyl; and when n represents 0 and B is 4-methylpiperidin-1-yl, B is not bromophenyl, chlorophenyl, methoxyphenyl, or tolyl.

4. (twice amended) The condensed pyridine compound as claimed in Claim 1, which is a compound represented by the following formula:



(wherein R<sup>31</sup> has the same meaning as that of the above R<sup>1</sup>, R<sup>32</sup> has the same meaning as that of the above R<sup>2</sup> and R<sup>33</sup> has the same meanings as that of the above B, respectively), its [pharmacologically] pharmaceutically acceptable salt or hydrates thereof.